Refractory Edema with CHF

Stepwise Approaches

Nephrology Perspectives

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Mansoura – March 2016

Talk Outline

- Pre-Diuresis Precautions
- Pre-Diuresis Lab/Imaging
- Bolus vs Continuous Infusion
- Single / Maximum Effective IV dose
- Intermittent IV Bolus Approach
- Continuous IV Infusion Approach
- Thiazides – When to add?
- Spironolactone – When to add?
- Hypertonic Saline at initiation
- Monitoring
- Switch to oral – When & How?

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Mechanism of Development of Refractory Edema

Prevents net fluid loss, <u>even with adequate therapeutic doses</u> of diuretics

Ellison DH. Ann Intern Med. 1991;114(10):886

Mechanism of Development of Refractory Edema

<u>24-hour urine:</u> A value above 100 mEq Na/day indicates noncompliance with sodium restriction

Ellison DH. Ann Intern Med. 1991;114(10):886.

Mechanism of Development of Refractory Edema

NSAIDs

Reduce the synthesis of prostaglandins

Ellison DH. Am J Kidney Dis. 1994;23(5):623

Pre-Diuresis Precautions:

- Ensure dietary sodium restriction
- Stop NSAIDs
- Exclude aminoglycosides

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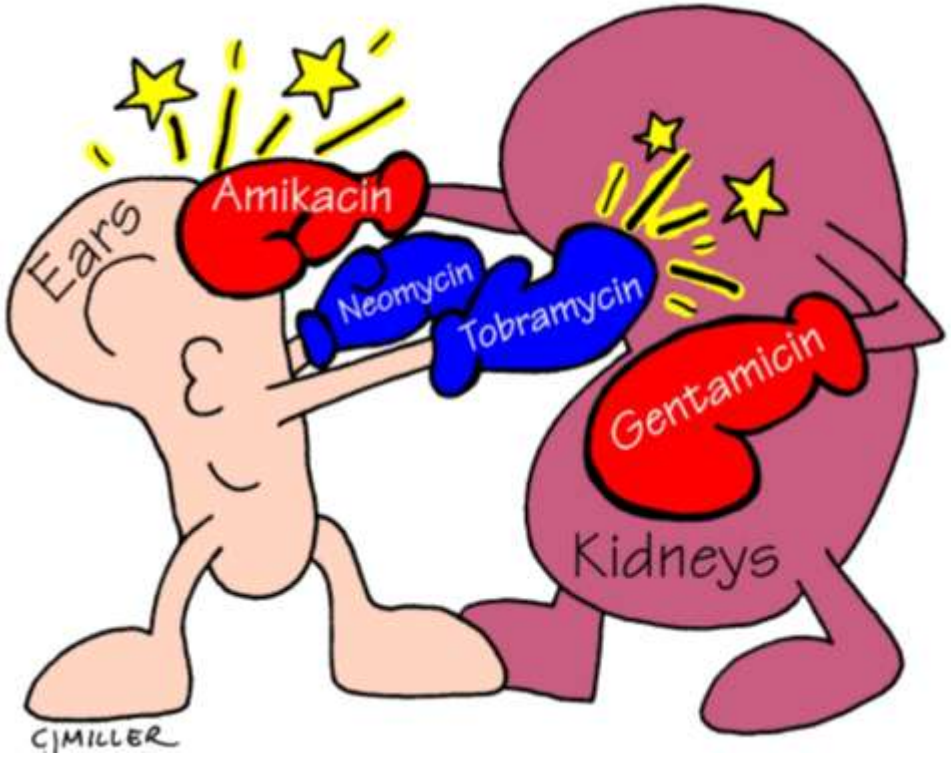

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Pre-Diuresis Precautions:

- Ensure dietary sodium restriction

- Stop NSAIDs

- Exclude aminoglycosides

Pre-Diuresis Lab: Serum Albumin, Urea/BUN, Creatinine, Na, K, Ca, Mg, Uric acid , Hb, Ht%

Other lab Ix (as indicated)

Pre-diuresis Imaging: CXR, USS Abdomen & Pelvis, ECHO

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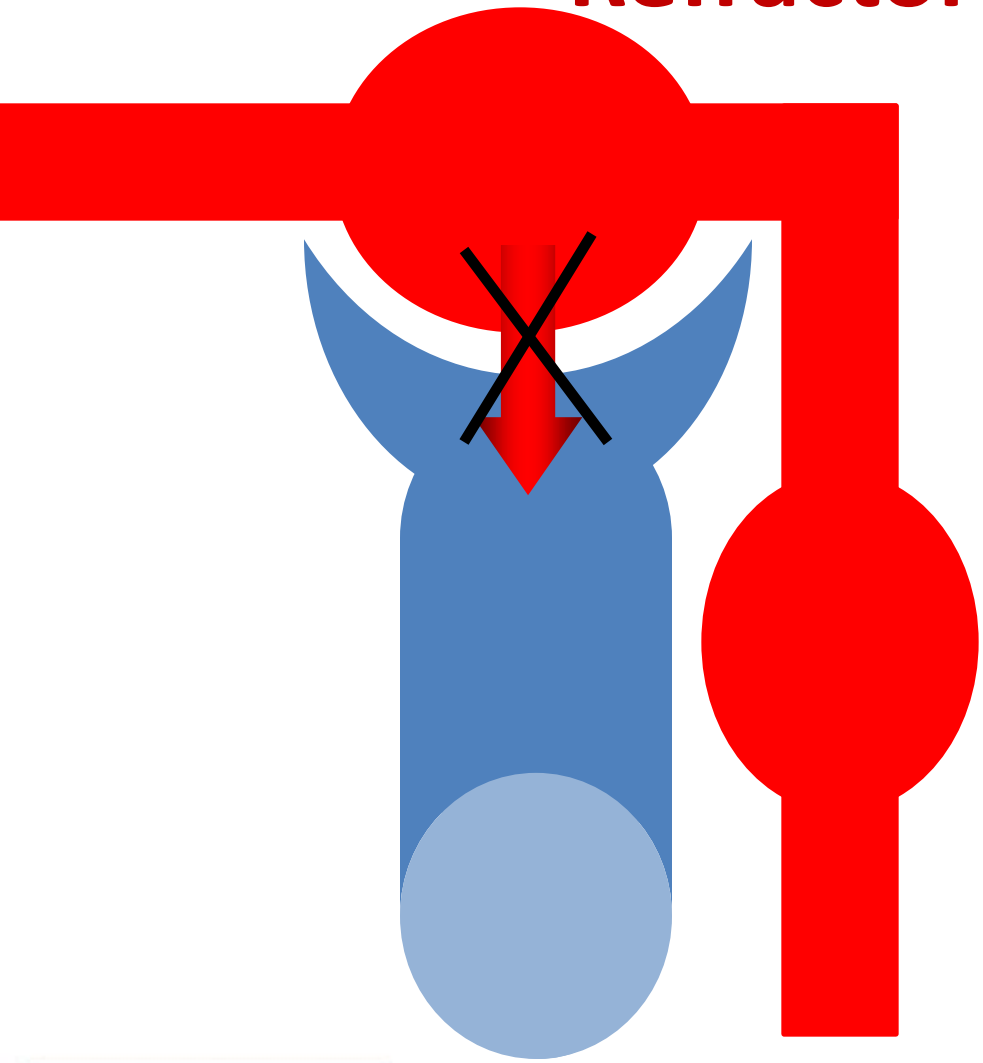

Hypoalbuminemia

Decreased loop diuretic secretion

Normal Loop Diuretics Secretion

NephroTube
Continuous Nephrology Education (CNE)
www.NephroTubeCNE.com

M.Gawad. www.NephroTubeCNE.com
Opie LH, Kaplan NM, Pool-Wilson P, eds. Drugs for the Heart. 5th edition. Diuretic therapy.

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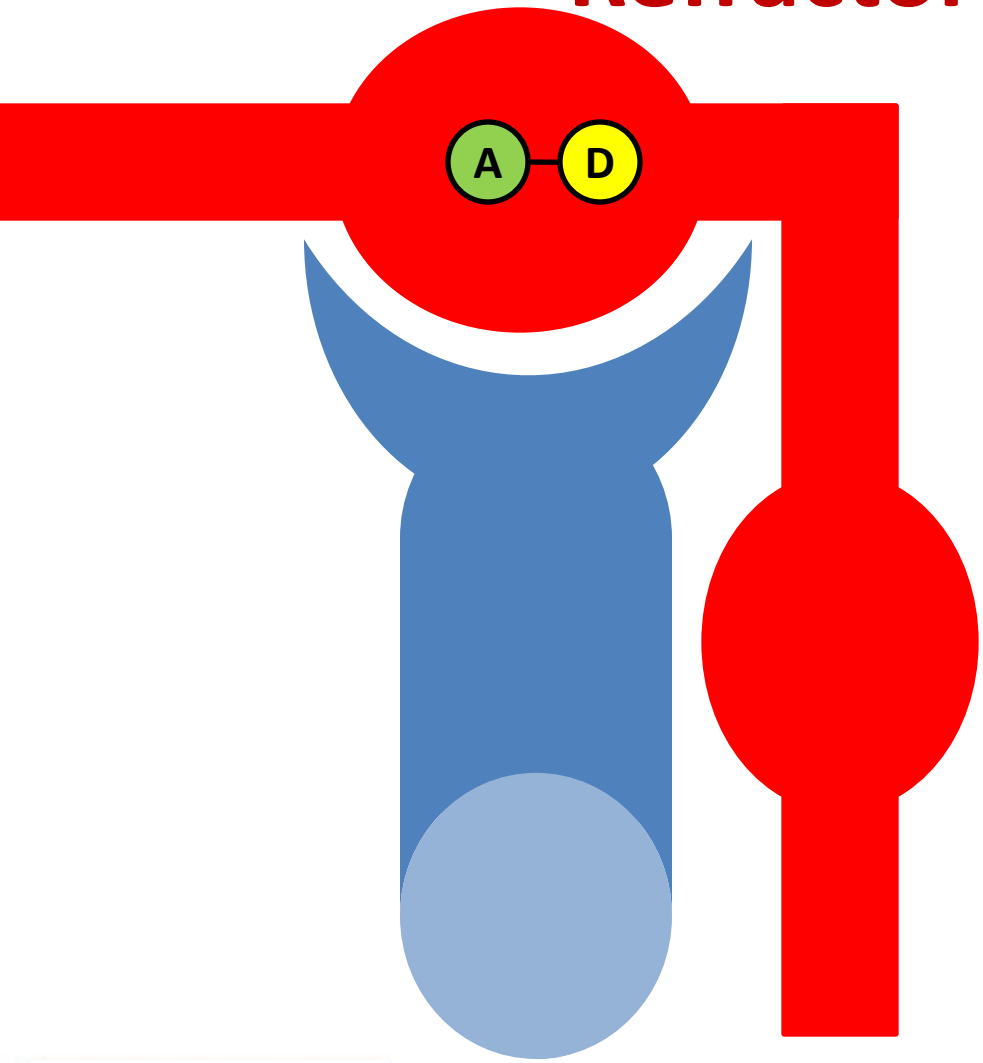

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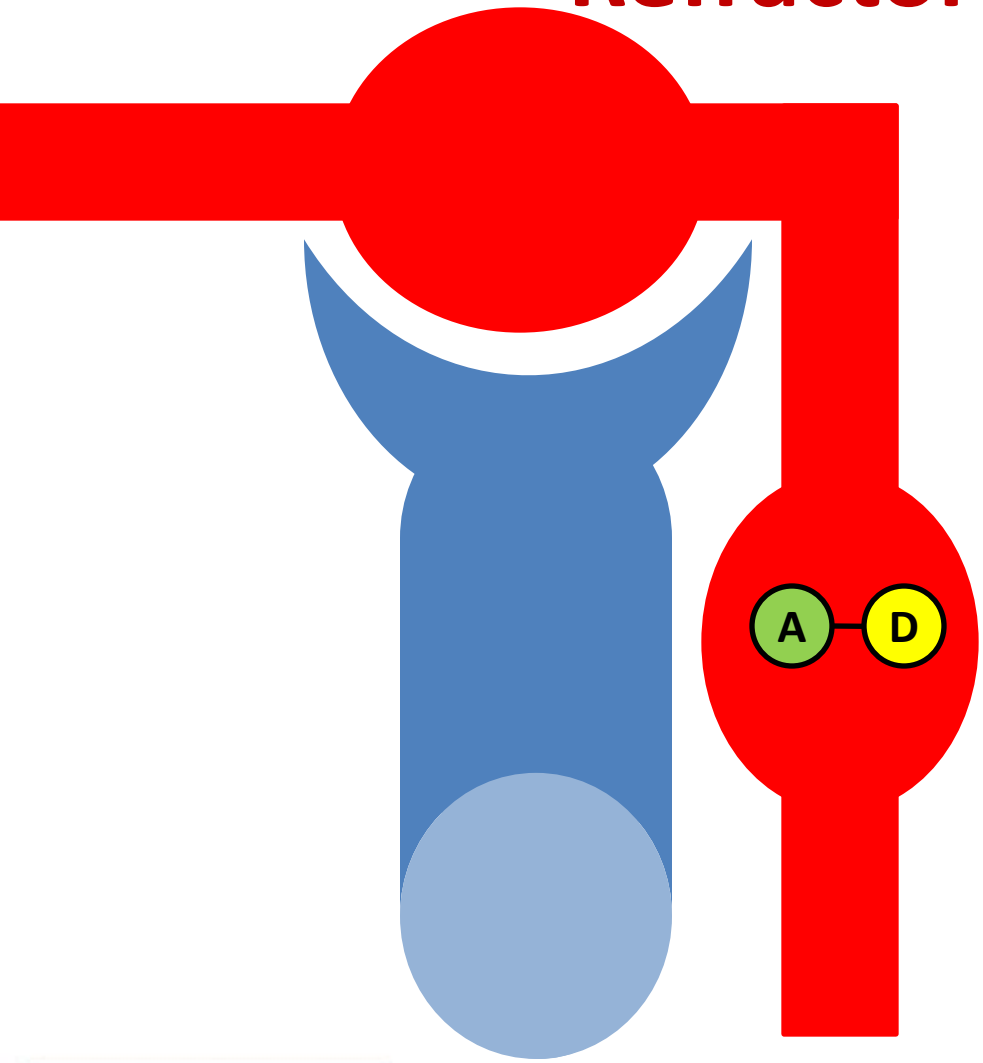

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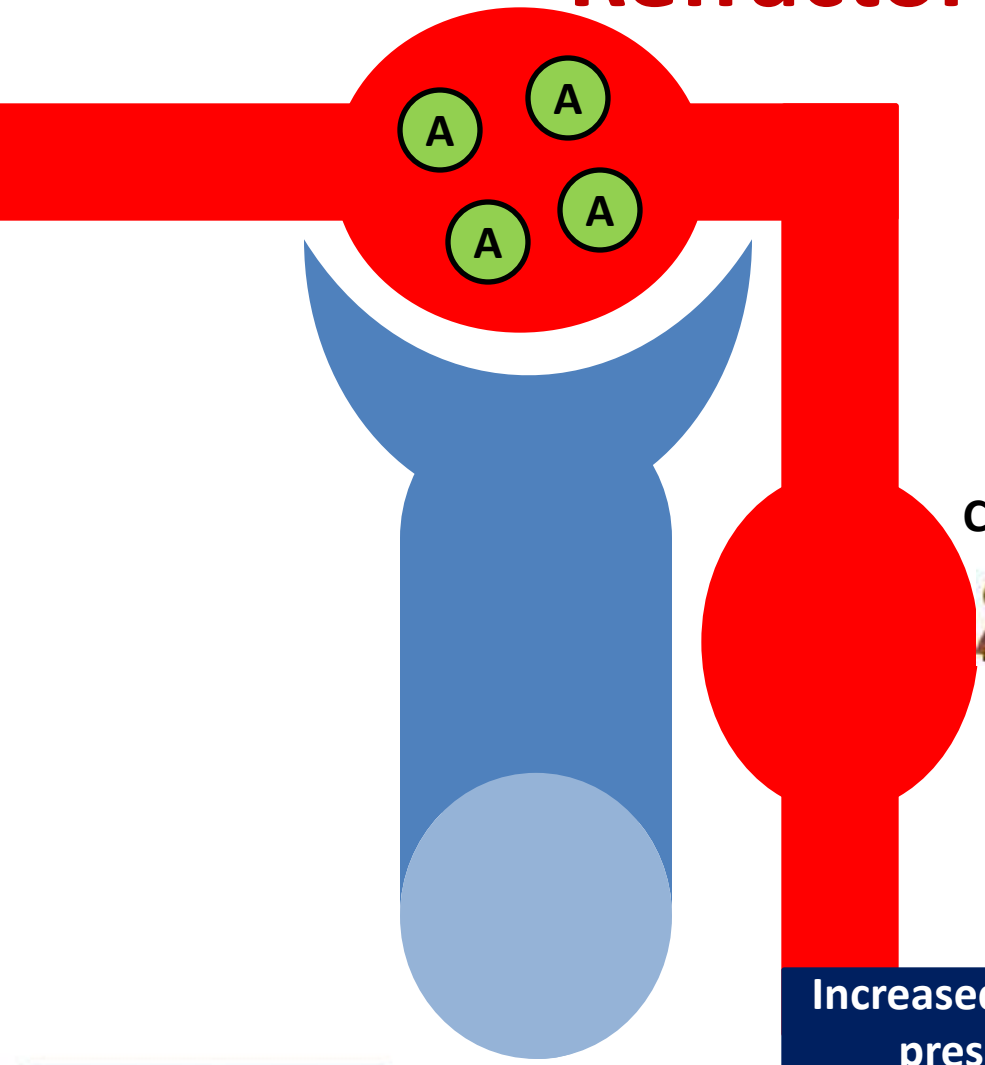

Hypoalbuminemia

Decreased loop diuretic secretion

Cardiac Cirrhosis

Mechanism of hypoalbuminemia in CHF

Increased venous pressure

Increased venous pressure

Heart CHF (low COP)

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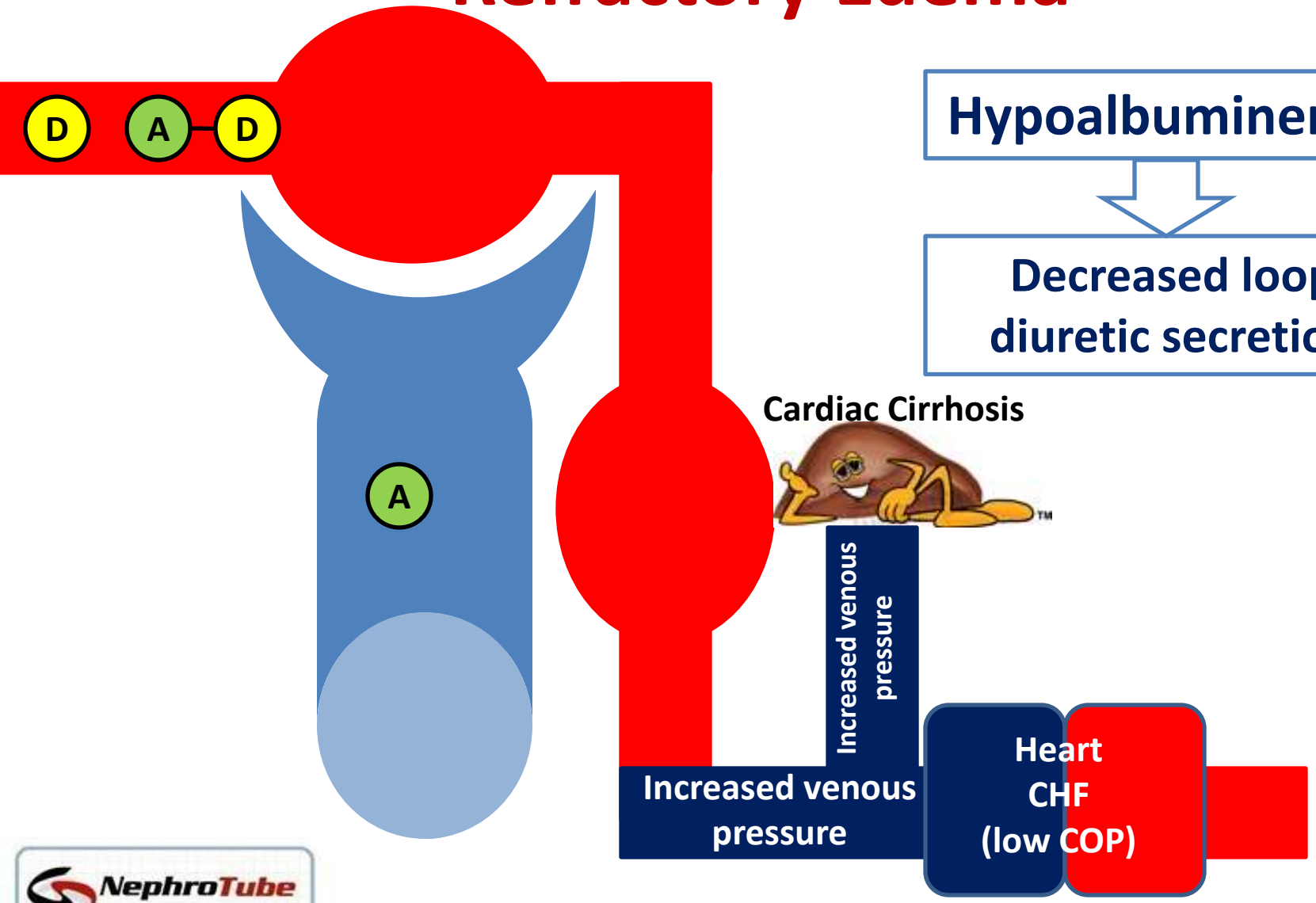

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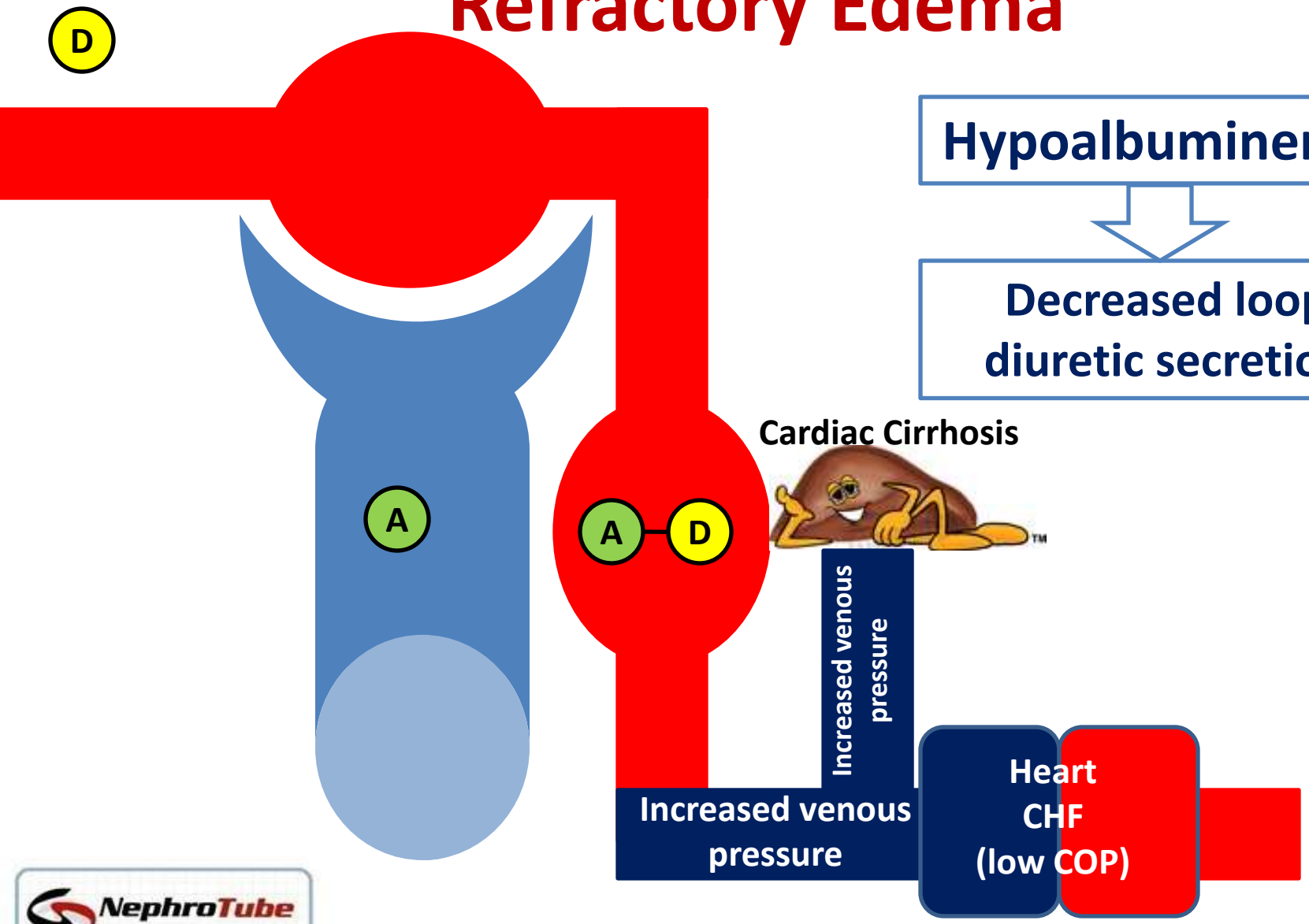

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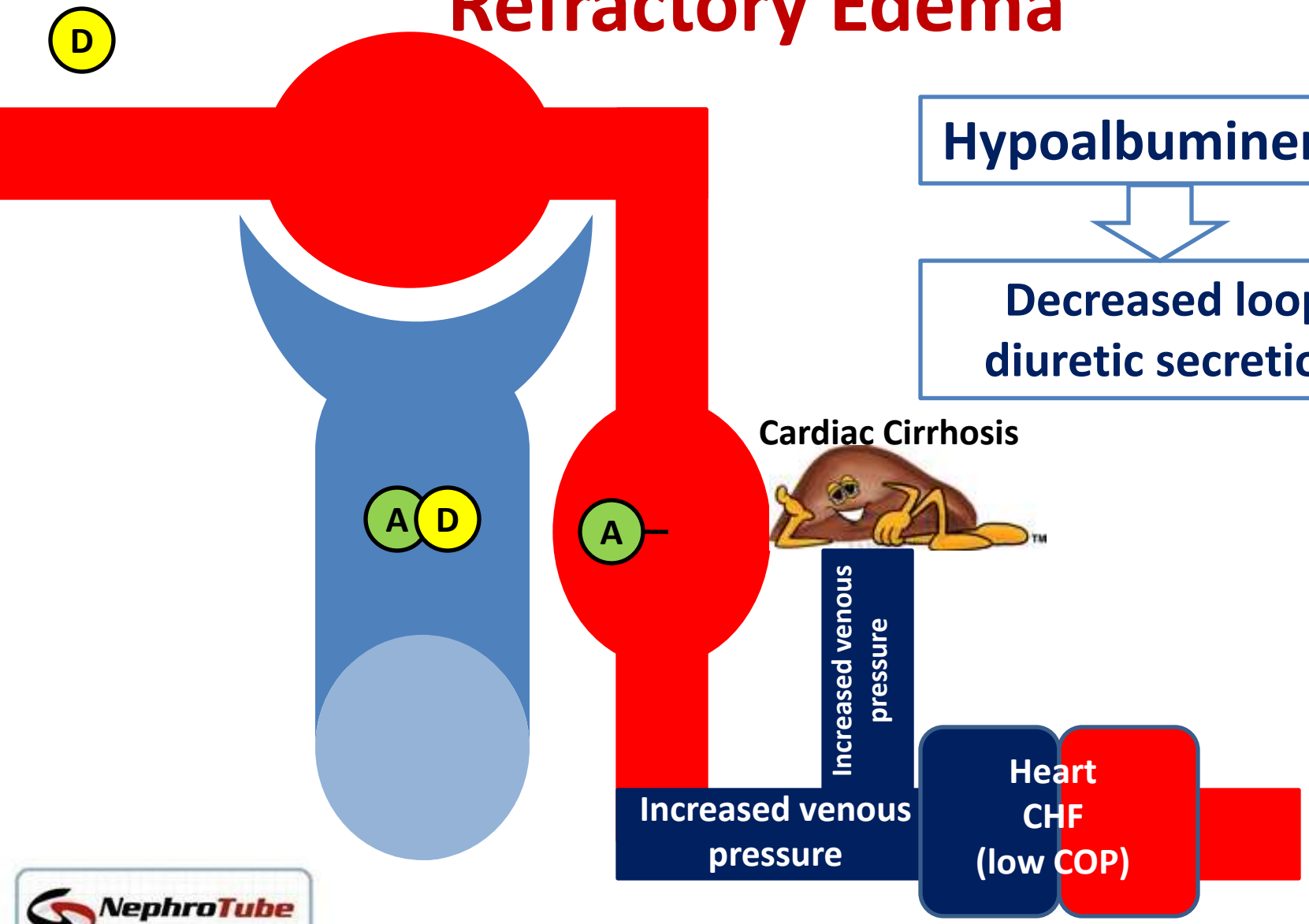

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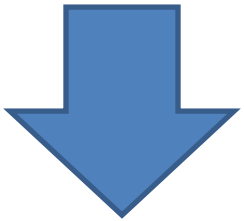
When to give Loop Diuretic + Albumin?

Loop diuretic + Albumin in hypoalbuminemic patients

(secondary to cirrhosis or nephrotic syndrome)

with mean plasma albumin 3.0 g/dL



No increase in the rate of furosemide excretion

Mutschler E et al. Kidney Int. 1999;55(2):629
Chalasani N et al. J Am Soc Nephrol. 2001;12(5):1010

When to give Loop Diuretic + Albumin?

Pre-Diuresis Precautions,

Pre-Diuresis Lab and Pre-diuresis Imaging

Albumin infusion

in case of hypoalbuminemia (<2 g/dl)

Evidence supporting this is weak as this has not been studied yet

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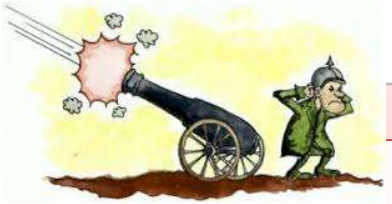
IV Diuretic Therapy



Intermittent
IV Bolus

Continuous
IV Infusion

Efficacy ??

Safety ??

Salvador DR et al. Cochrane Database Syst Rev. 2005; :CD003178
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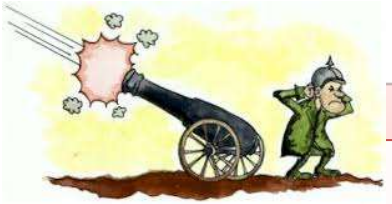

Intermittent IV Bolus

Continuous IV Infusion

Efficacy ?? → **Similar efficacy**

Safety ??

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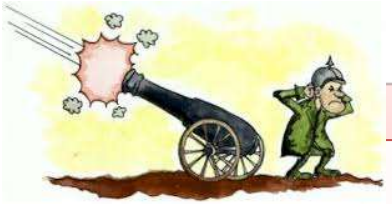

Intermittent IV Bolus

Continuous IV Infusion

Efficacy ?? → **Similar efficacy**

Safety ?? → **Continuous IV is safer** *(less ototoxicity)*

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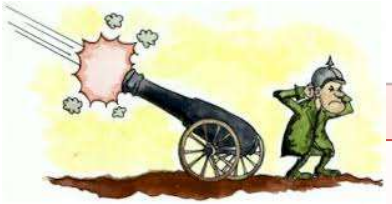
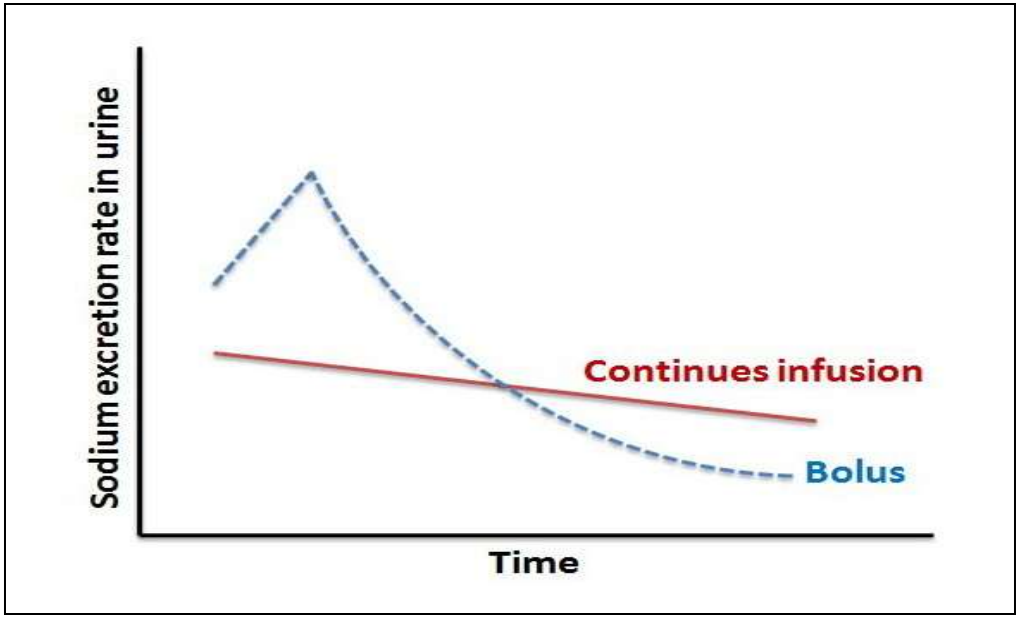


Intermittent IV Bolus

Continuous IV Infusion



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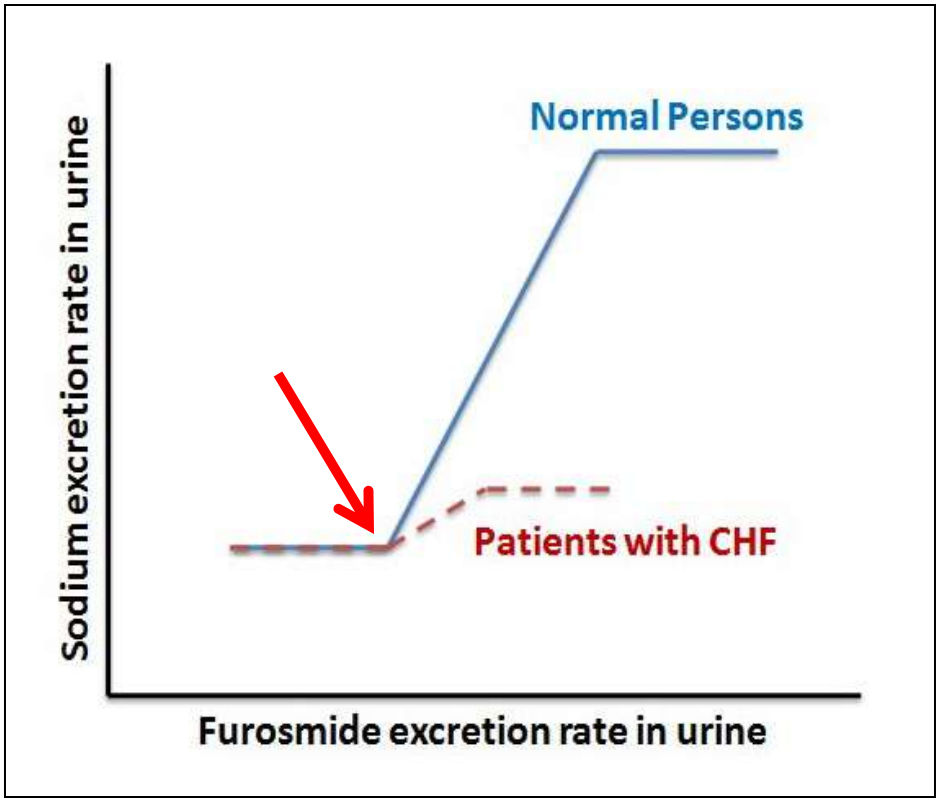
SINGLE IV Effective Dose (Loop Diuretics)

No natriuresis seen until a threshold rate of drug excretion in urine is attained



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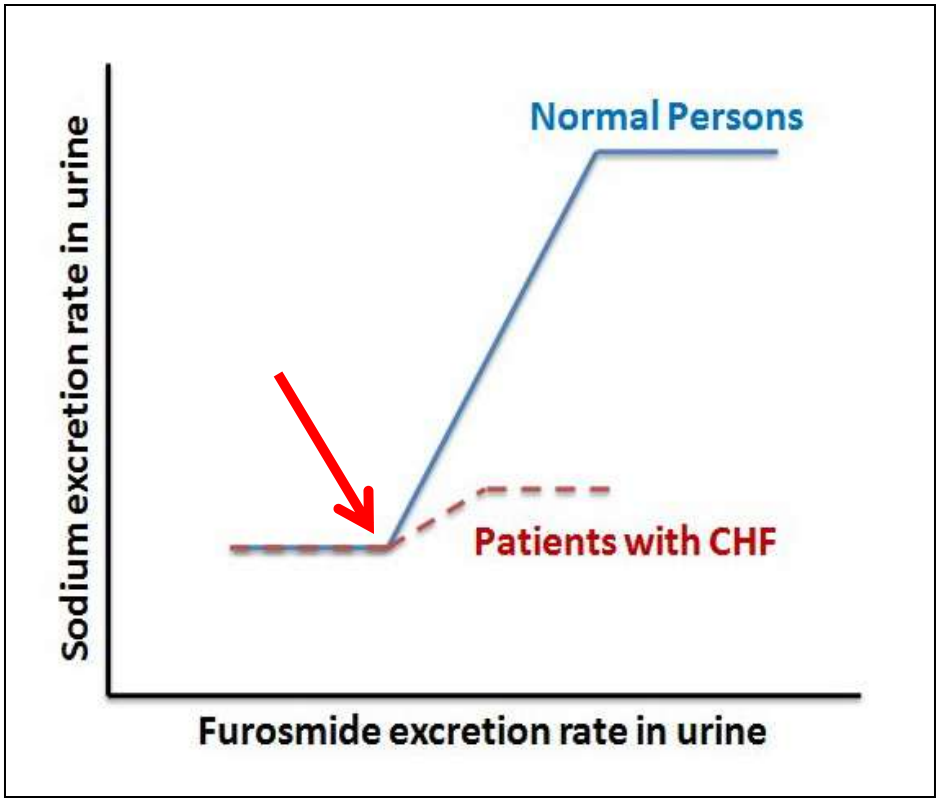
SINGLE IV Effective Dose (Loop Diuretics)

No diuresis to 40 mg of furosemide



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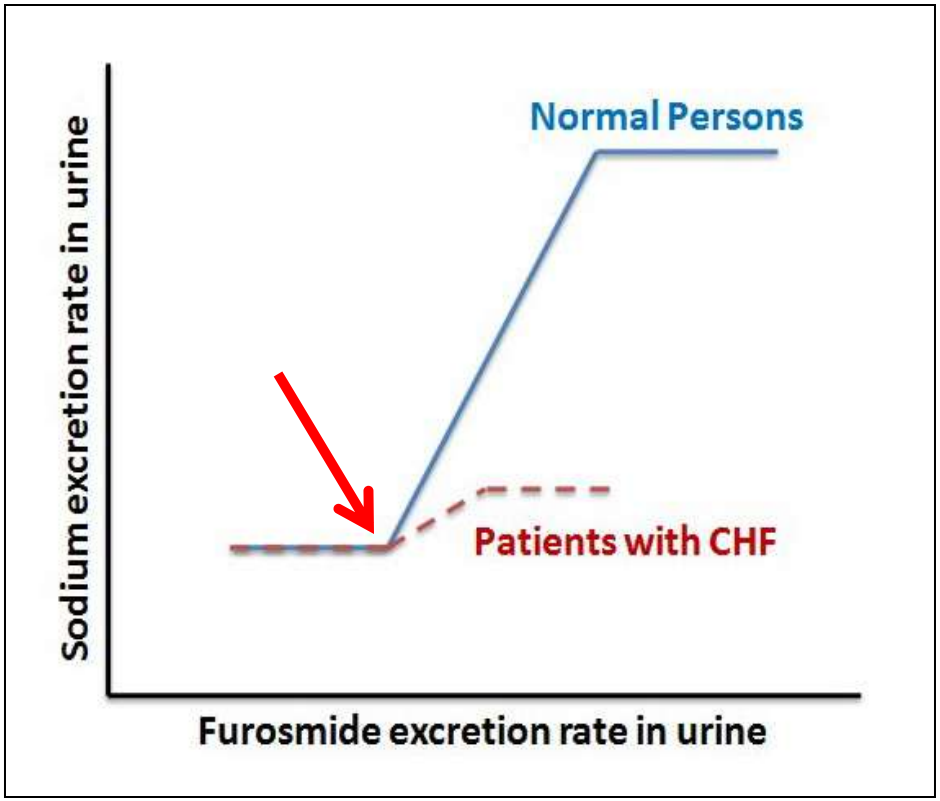
SINGLE IV Effective Dose (Loop Diuretics)

So simply, single effective dose is **the least dose** that will cause **response** i.e. diuresis.



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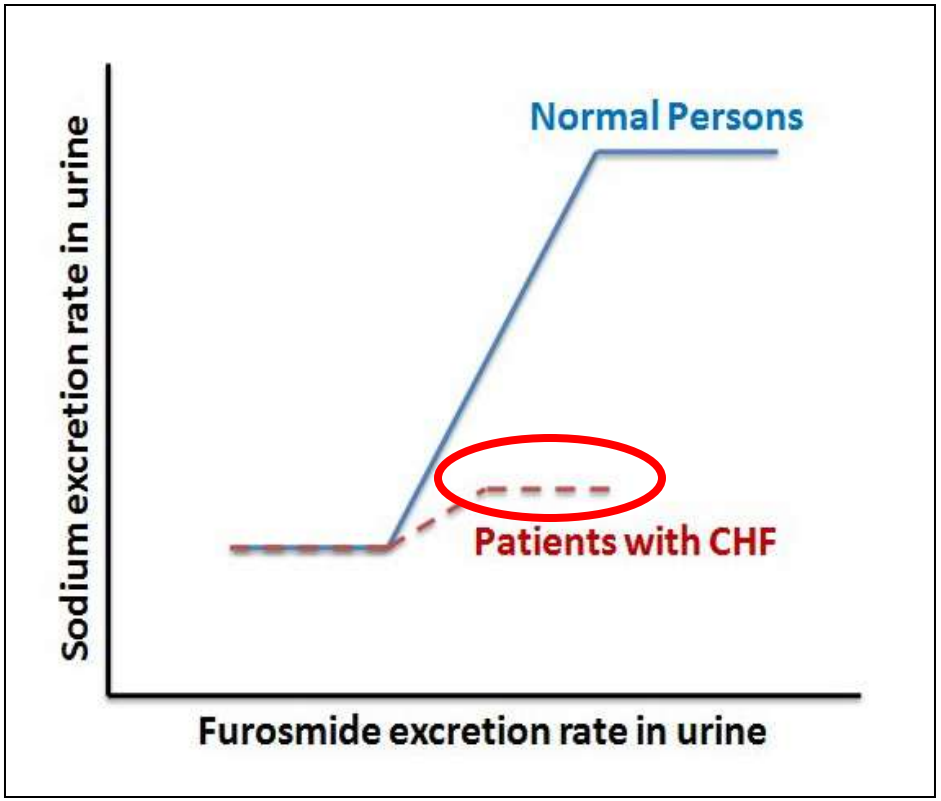
MAXIMUN IV Effective Dose (Loop Diuretics)

The dose at which loop Na-Cl transport is completely inhibited

Administering higher doses will produce little or no further diuresis,

a plateau is reached



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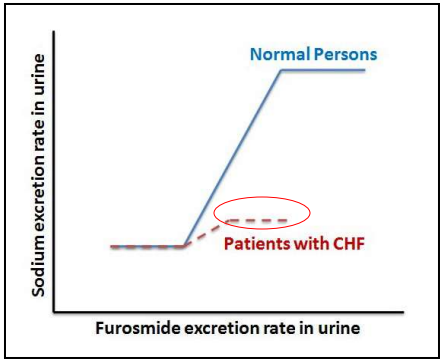

Maximum IV Effective Dose

Normal eGFR	Moderate CKD	Severe CKD	
40 mg (over 5 minutes) to 80 mg (over 20 minutes) of furosemide, 1 to 2 mg of bumetanide, 20 to 40 mg of torsemide.	80 mg of furosemide (over 20 minutes), 2 to 3 mg of bumetanide, 20 to 50 mg of torsemide.	200 mg (over 40 to 50 minutes) of furosemide, 8 to 10 mg of bumetanide 50 to 100 mg of torsemide.	ACC/AHA recommendations: 160 to 200 mg (over 40 to 50 minutes) of furosemide, 4 and 8 mg of bumetanide 100 to 200 mg of torsemide

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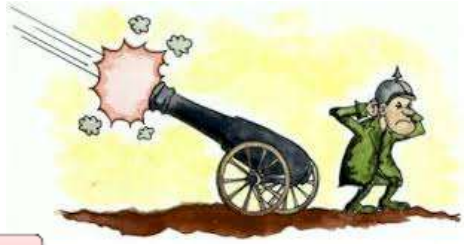
Intermittent IV Bolus

Pre-Diuresis Precautions,

Pre-Diuresis Lab and Pre-diuresis Imaging

Albumin infusion in case of hypoalbuminemia (<2 g/dl)



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Continuous IV Infusion

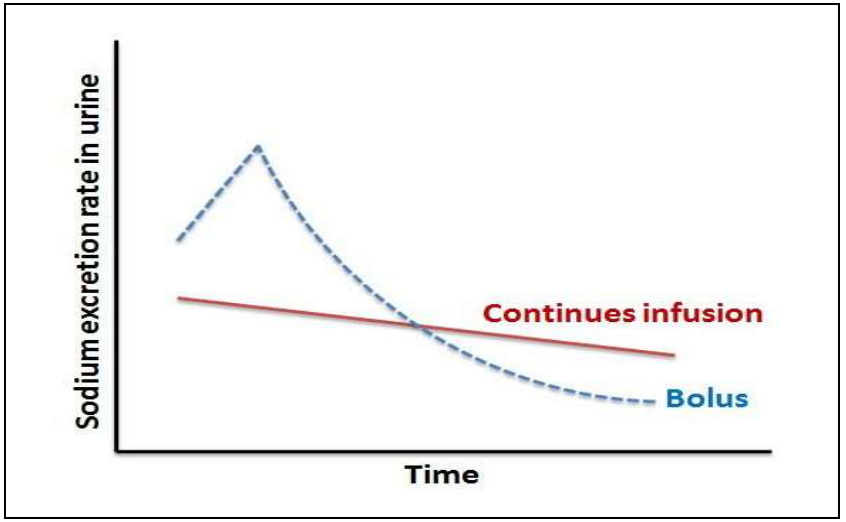
Pre-Diuresis Precautions,

Pre-Diuresis Lab and Pre-diuresis Imaging

Albumin infusion in case of hypoalbuminemia (<2 g/dl)

IV loading bolus dose of furosemide (or equivalent)

(Starting by single effective dose up to maximum effective dose)



Continuous IV infusion should not be tried in patients who have not responded to repeated bolus doses

(up to maximum effective dose)

Dormans TP et al. J Am Coll Cardiol. 1996;28(2):376
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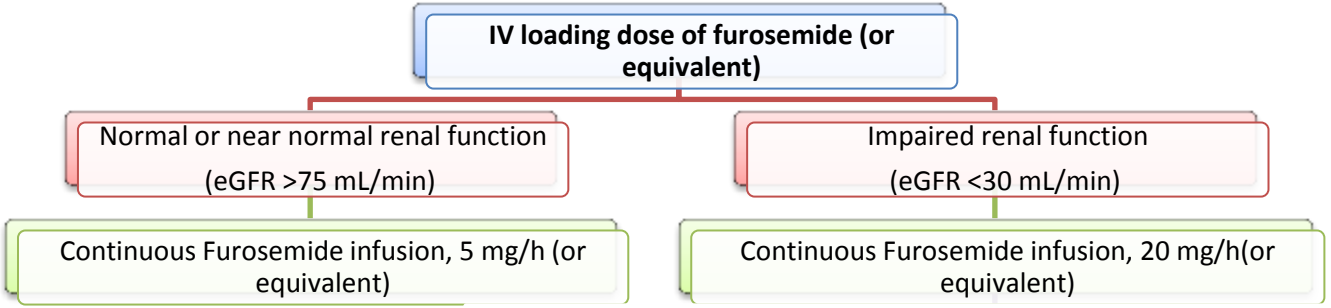

Continuous IV Infusion

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Hunt SA et al. Circulation. 2009;119(14):e391
Brown CB et al. Clin Nephrol. 1981;15(2):90
Brater DC. N Engl J Med. 1998;339(6):387
Gallagher KL, Jones JK. Ann Intern Med. 1979;91(5):744.

Continuous IV Infusion

IV loading dose of furosemide (or equivalent)

- Normal or near normal renal function (eGFR >75 mL/min)
  - Continuous Furosemide infusion, 5 mg/h (or equivalent)
- Impaired renal function (eGFR <30 mL/min)
  - Continuous Furosemide infusion, 20 mg/h(or equivalent)

Follow Up UOP after 2 hrs:
Minimal required UOP: 0.5-1 ml/kg/h, which can be increased according clinical situation

- Inadequate or NO UOP
  - a **second bolus** is given followed by a **higher infusion rate** of 10 mg/h **± Thiazide Initial dose**
  - **Follow Up UOP after 2 hrs**
    - **If inadequate or No UOP: a second bolus** is given followed by **a higher infusion rate** of 20 mg/h up to 4 mg/min (but the risk of ototoxicity and other side effects is high) **± Thiazide maximum dose**
    - **Follow Up UOP after 2 hrs**
      - No UOP
        - UF
- Adequate UOP
  - Assess UOP every 2 hrs
  - Increase or decrease infusion rate according to monitoring parameters
  - Convert to oral therapy

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Equivalent doses of other loop diuretics to furosemide dose

Furosemide IV	Torsemide IV / PO	Bumetanide IV / PO
20 mg	10 mg	1 mg
40 mg	20 mg	2 mg

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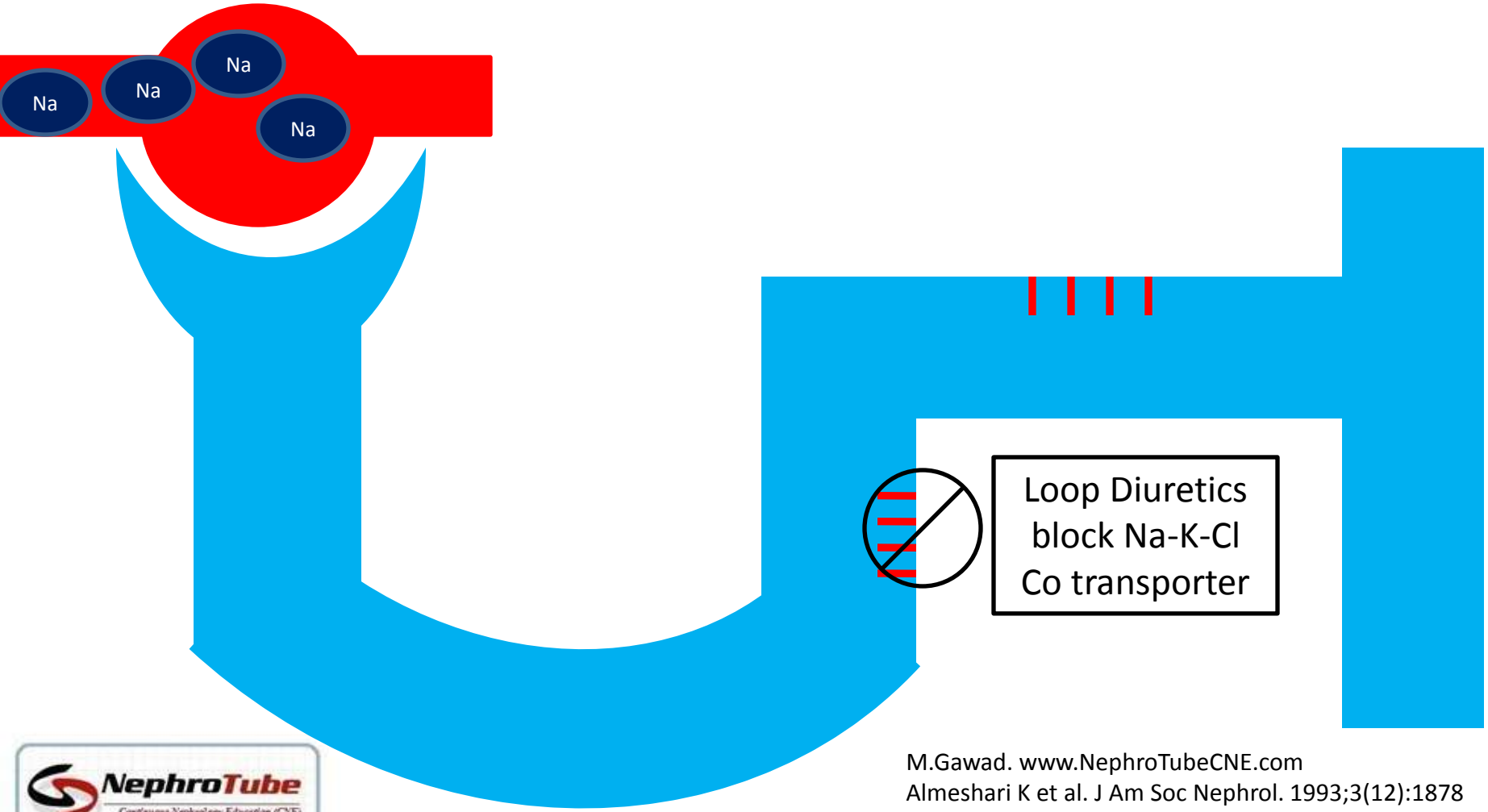
When to Add Thiazide Diuretic?



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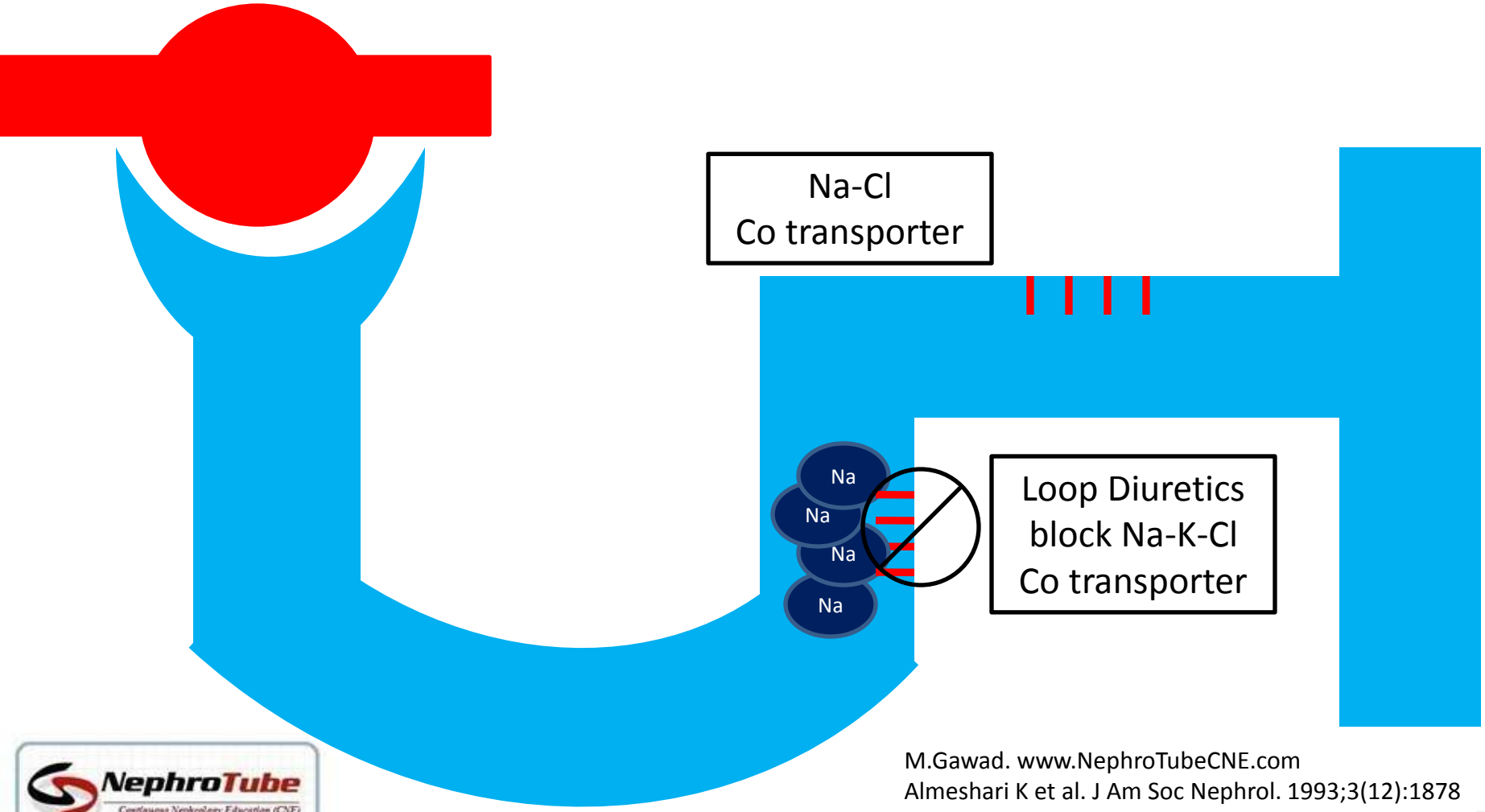

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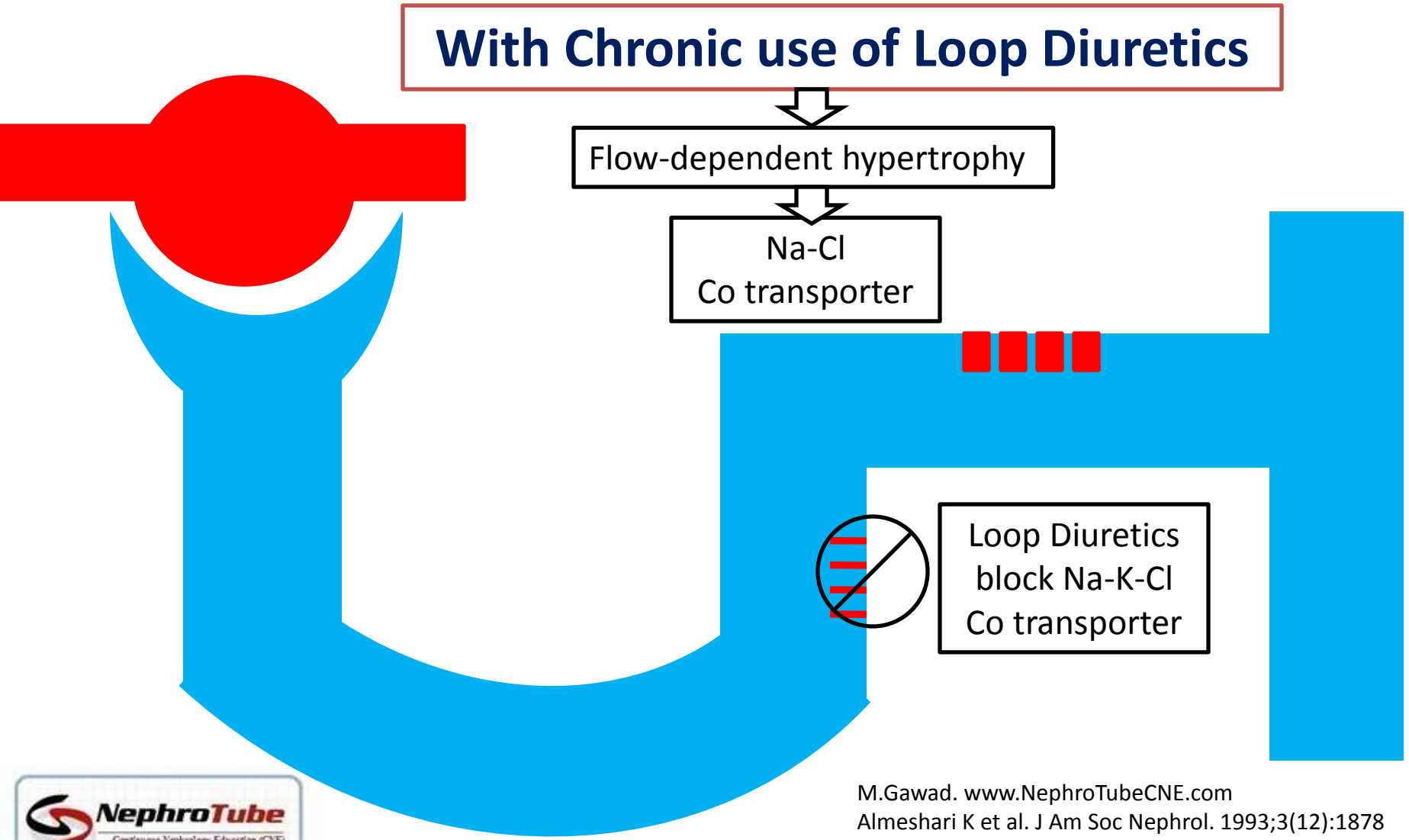
When to Add Thiazide Diuretic?



M.Gawad. www.NephroTubeCNE.com
Almeshari K et al. J Am Soc Nephrol. 1993;3(12):1878
Abdallah JG et al. J Am Soc Nephrol. 2001;12(7):1335
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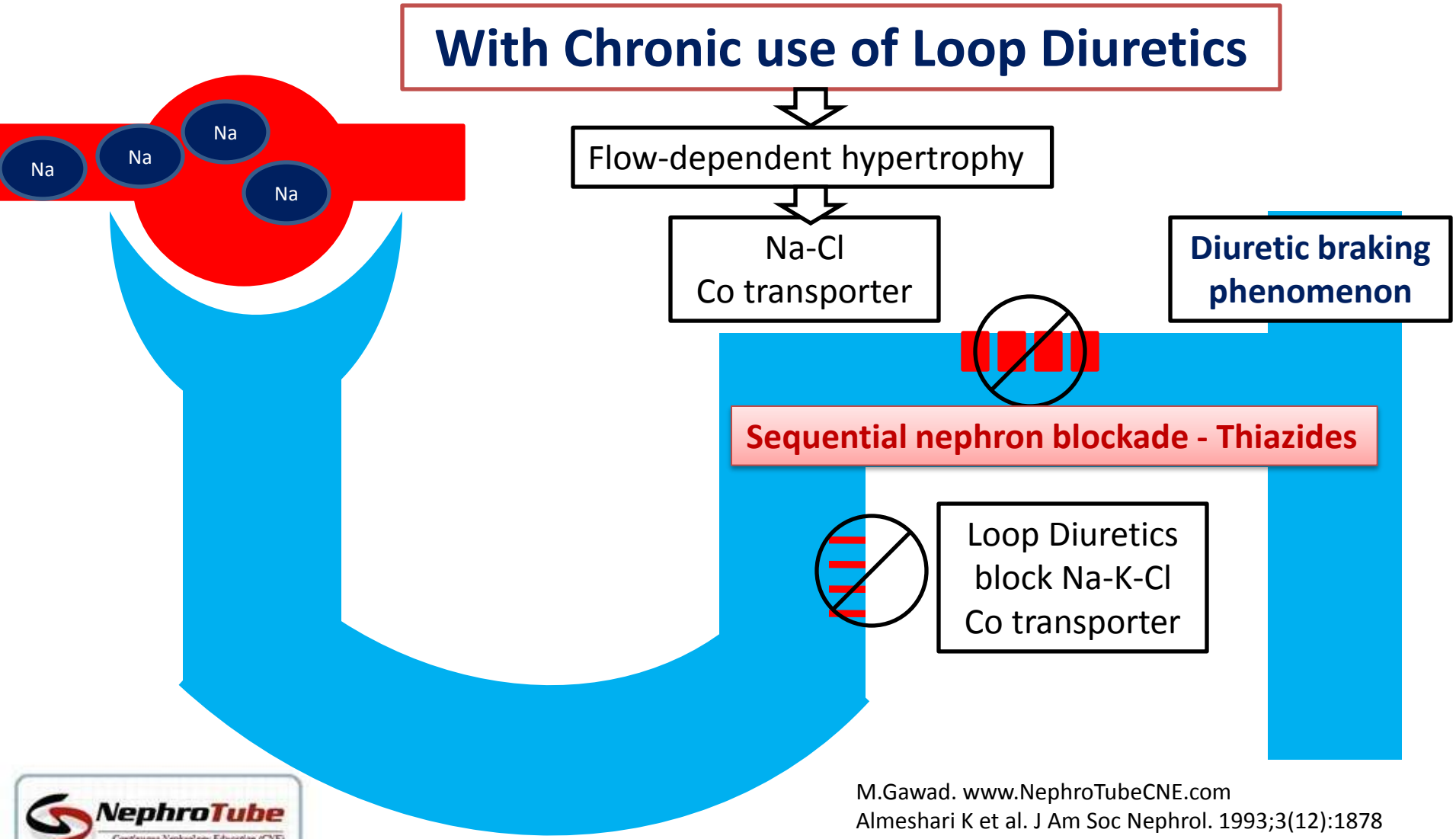

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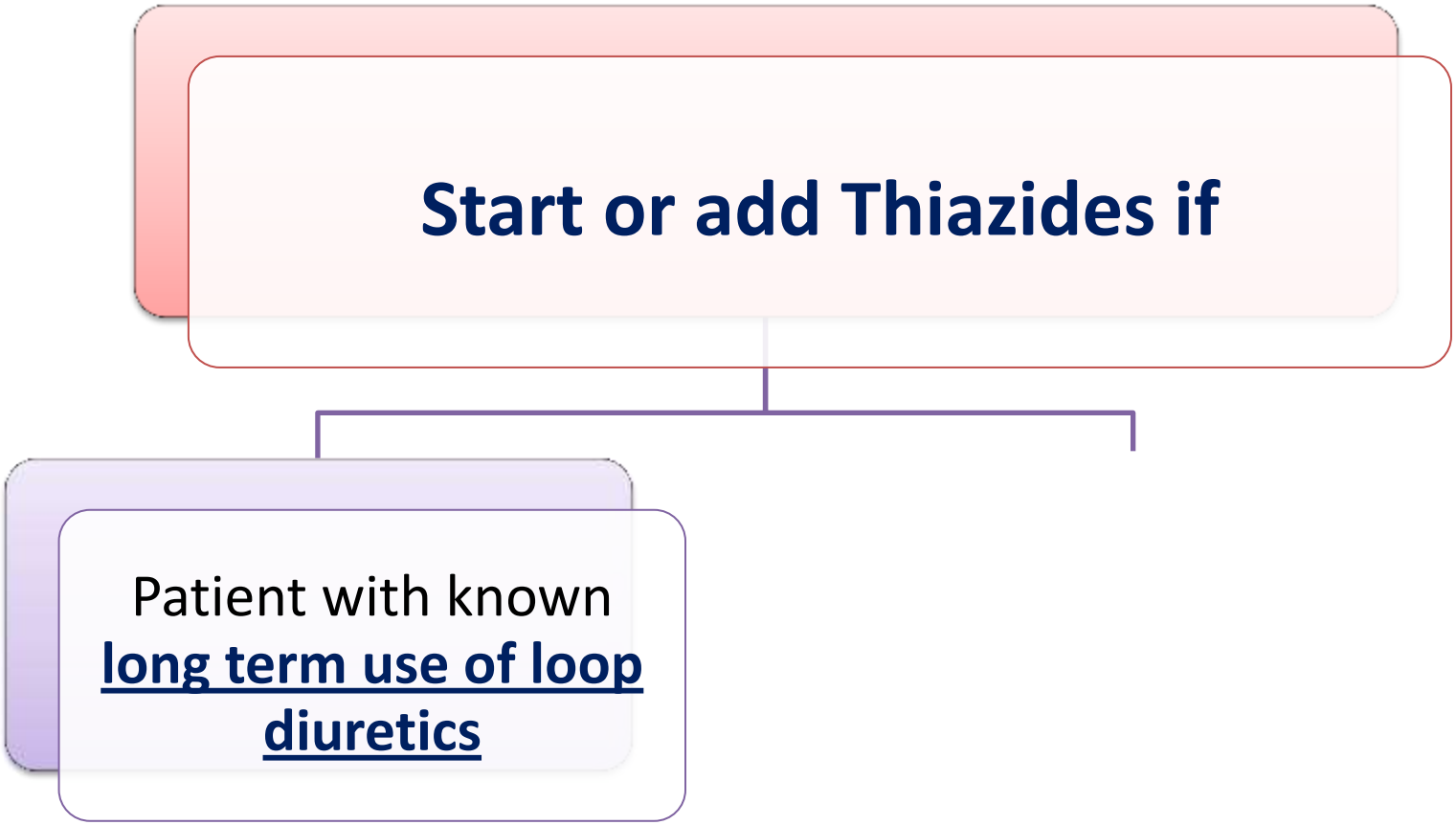
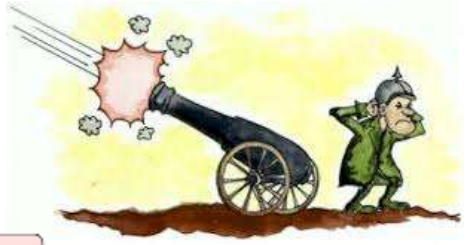


Intermittent IV Bolus



Pre-Diuresis Precautions,

Pre-Diuresis Lab and Pre-diuresis Imaging

Albumin infusion in case of hypoalbuminemia (<2 g/dl)

Initial intravenous bolus dose of furosemide is 20 to 40 mg (or equivalent)

Good response	No response to initial bolus dose	Partial diuretic response to once daily single effective or maximum bolus dose
Continue the same dose with follow up	Double the dose every 2 hrs as needed up to the maximum recommended doses	- Repeat loop diuretic dose twice or even three times a day - Add thiazide diuretic ??

Gawad. UNOAJ. Volume 1, Issue 2 – November, 2014
Almeshari K et al. J Am Soc Nephrol. 1993;3(12):1878
Rudy DW et al Ann Intern Med. 1991;115(5):360.
Brater DC, Voelker JR. In: Pharmacotherapy of Renal Disease and Hypertension, New York 1987. Vol 17.

Continuous IV Infusion

IV loading dose of furosemide (or equivalent)

- Normal or near normal renal function (eGFR >75 mL/min)
  - Continuous Furosemide infusion, 5 mg/h (or equivalent)
- Impaired renal function (eGFR <30 mL/min)
  - Continuous Furosemide infusion, 20 mg/h(or equivalent)

Follow Up UOP after 2 hrs:

Minimal required UOP: 0.5-1 ml/kg/h, which can be increased according clinical situation

- Inadequate or NO UOP
  - a **second bolus** is given
  - followed by a **higher infusion rate** of 30 mg/h
  - **± Thiazide Initial dose**
  - **Follow Up UOP after 2 hrs**
    - **If inadequate or No UOP: a second bolus** is given
    - followed by **a higher infusion rate** of 40 mg/h up to 4 mg/min (but the risk of ototoxicity and other side effects is high)
    - **± Thiazide maximum dose**
    - **Follow Up UOP after 2 hrs**
      - No UOP
        - UF
- Adequate UOP
  - Assess UOP every 2 hrs
  - Increase or decrease infusion rate according to monitoring parameters
  - Convert to oral therapy

Gawad. UNOAJ. Volume 1, Issue 2 – November, 2014
Hunt SA et al. Circulation. 2009;119(14):e391
Brown CB et al. Clin Nephrol. 1981;15(2):90
Brater DC. N Engl J Med. 1998;339(6):387
Gallagher KL, Jones JK. Ann Intern Med. 1979;91(5):744.

Talk Outline

- Pre-Diuresis Precautions
- Pre-Diuresis Lab/Imaging
- Bolus vs Continuous Infusion
- Single / Maximum Effective IV dose
- Intermittent IV Bolus Approach
- Continuous IV Infusion Approach
- Thiazides – When to add?
- Spironolactone – When to add?
- Hypertonic Saline at initiation
- Monitoring
- Switch to oral – When & How?

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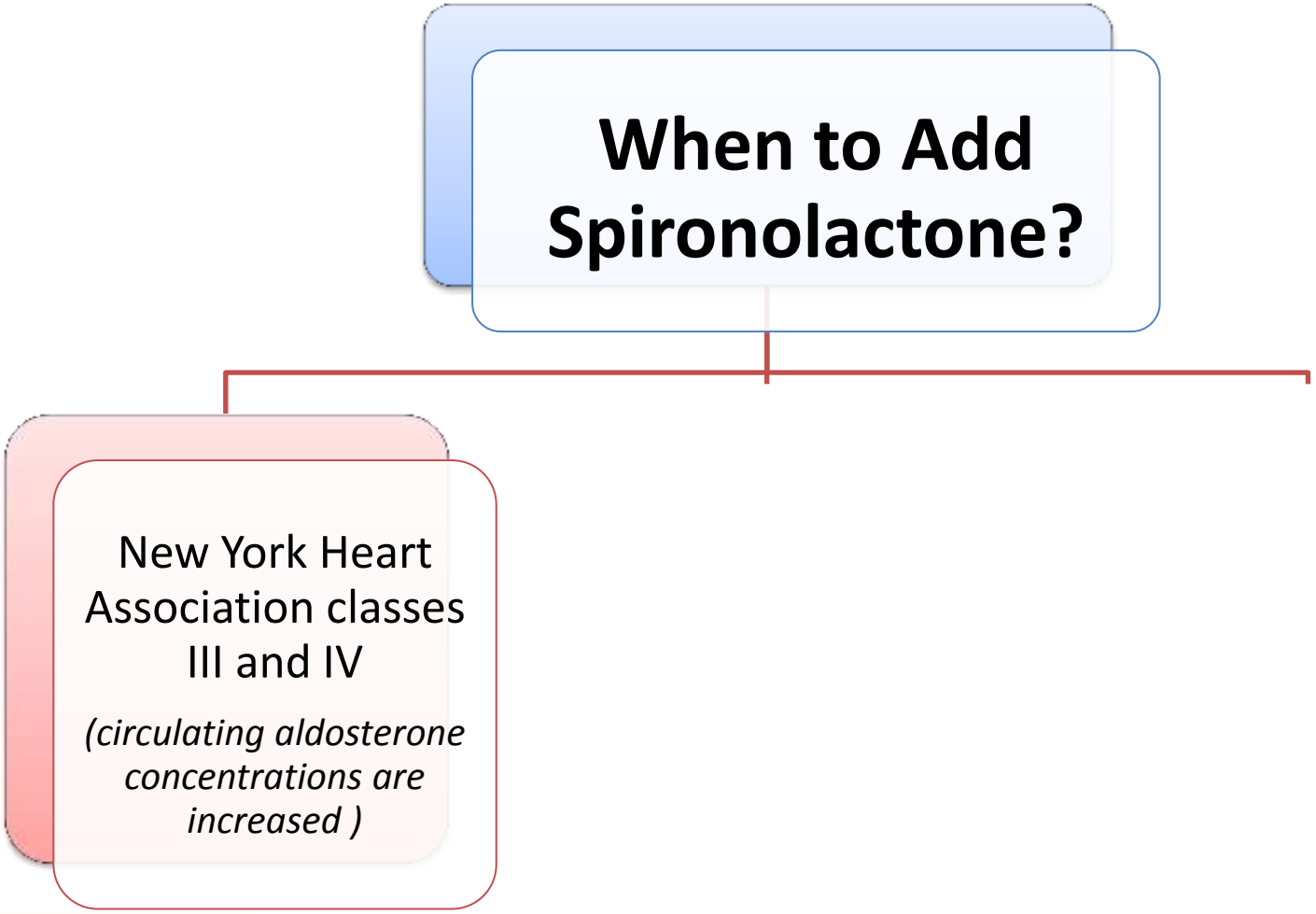
When to Add Spironolactone?



Fliser D et al. Kidney Int. 1994;46(2):482.
Pitt B et al. N Engl J Med. 1999;341:709-716.

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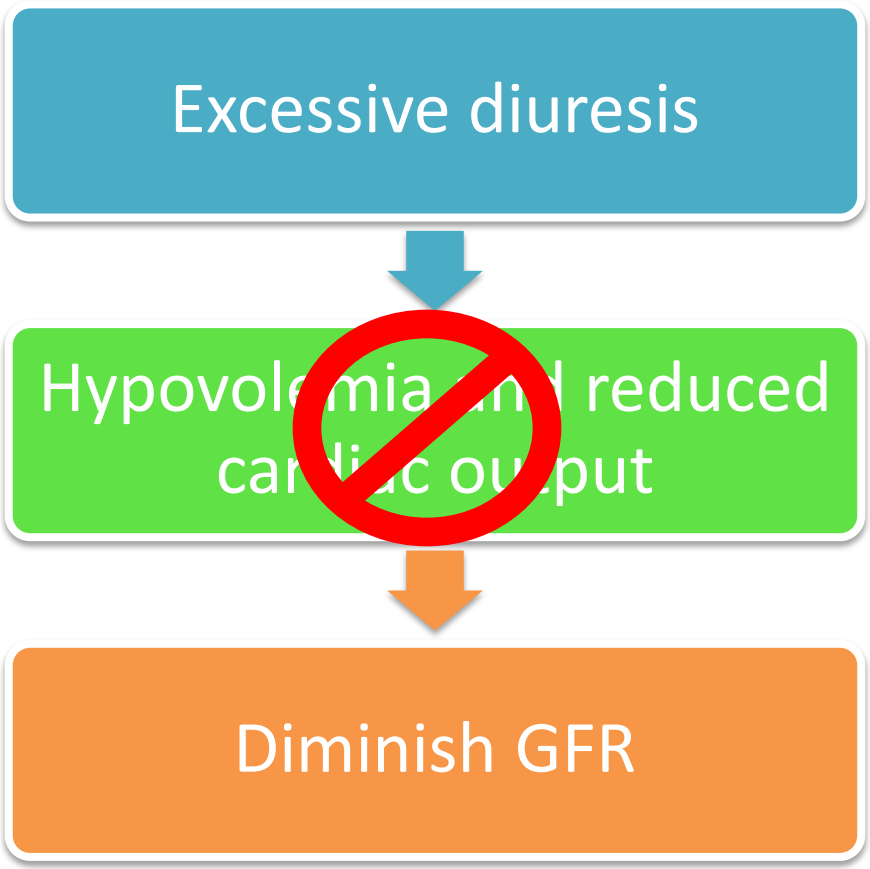
IV High-Dose Furosemide and Hypertonic Saline Solutions

Pre-Diuresis Precautions,

Pre-Diuresis Lab and Pre-diuresis Imaging

Albumin infusion in case of hypoalbuminemia (<2 g/dl)

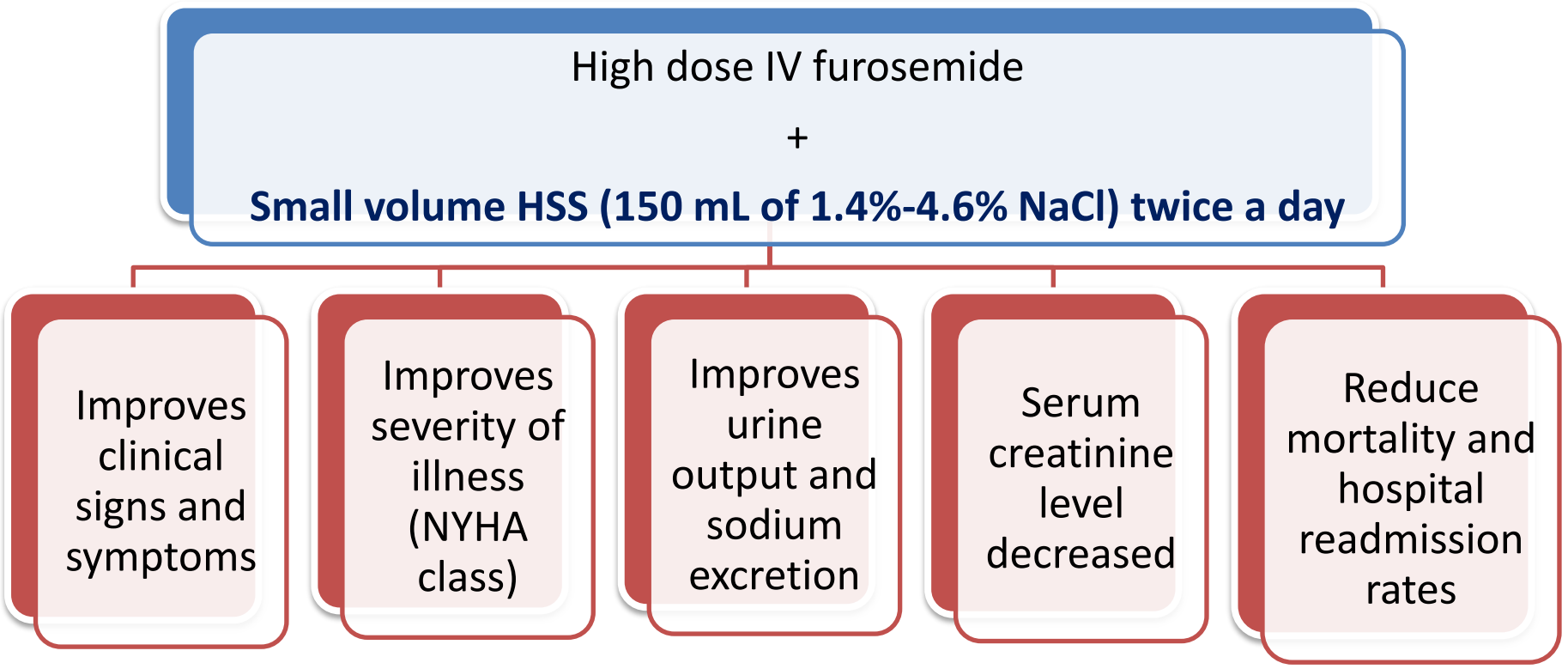
IV High-Dose Furosemide and Hypertonic Saline Solutions



Maintaining an **adequate intravascular volume** will maintain good renal perfusion

Nieminen MS, Bohm M, Cowie MR, et al. Eur Heart J. 2005;26:384-416.

IV High-Dose Furosemide and Hypertonic Saline Solutions



Nieminen MS et al. Eur Heart J. 2005;26:384-416.
Paterna S et al. Adv Ther. 1999;16:219-28.
Paterna S et al. Eur J Heart Fail. 2000;2:305-13.
Licata Get al. Am Heart J. 2003;145:459-66

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Monitoring

Lab:	• Na, K (daily) • Urea/BUN, Creatinine (daily) • Hb, Ht% (daily) • ABG • Ca, Mg • Uric Acid • Serum Albumin • Other lab Ix (as indicated)
Radiology (as needed):	• CXR • USS Abdomen & Pelvis • ECHO

Monitoring

Clinical:	**Weight measurement**: should be performed at the same time each day, usually in the morning, prior to eating and after voiding

Talk Outline

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Switching from IV to Oral Loop Diuretics

When to start?	It depends on the clinical decision of the treating physician.

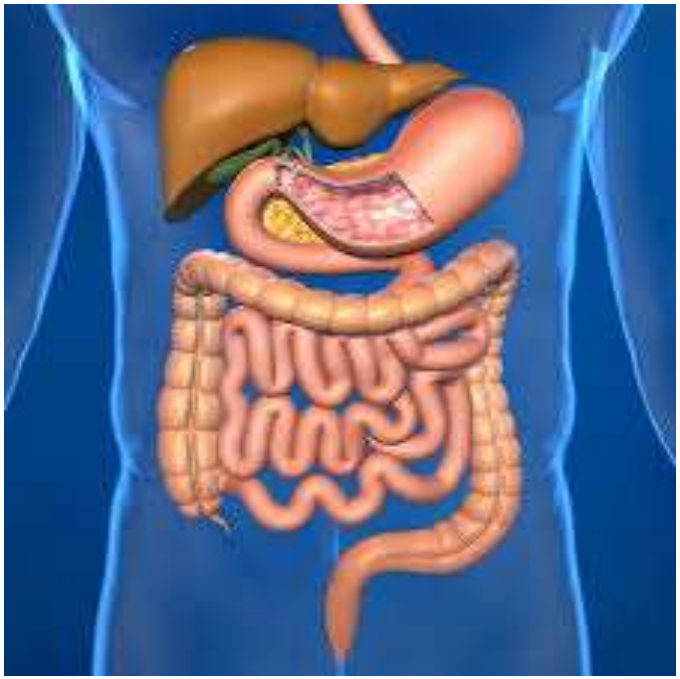
Decreased intestinal perfusion

Reduced intestinal motility

Intestinal mucosal edema

↓

Reduce the diuretic absorption

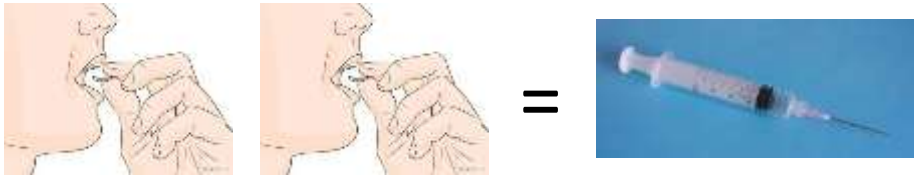


Krämer BK, Schweda F, Riegger GA. Am J Med. 1999;106(1):90

Switching from IV to Oral Loop Diuretics

Dosage	• The oral dose of Furosemide is approximately twice the intravenous dose. • The oral dose of Torsemide & Bumetanide is the same as the intravenous dose.

Furosemide



Torsemide & Bumetanide

Hunt SA et al. Circulation. 2009;119(14):e391
Wargo KA, Banta WM. Ann Pharmacother. 2009;43(11):1836

Take Home Messages

Pre-diuresis precautions to exclude reversible predisposing factors of resistance

Pre-Diuresis Precautions:

- Ensure dietary sodium restriction
- Stop NSAIDs
- Exclude aminoglycosides

Pre-diuresis Ix as a base line for follow up

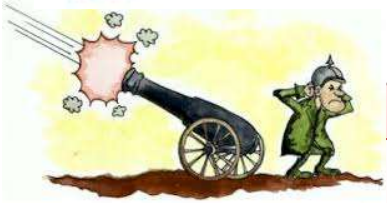
Pre-Diuresis Lab: Serum Albumin, Urea/BUN, Creatinine, Na, K, Ca, Mg, Uric acid , Hb, Ht%
Other lab Ix (as indicated)

Pre-diuresis Imaging: CXR, USS Abdomen & Pelvis, ECHO.

Albumin infusion in case of hypoalbuminemia (<2 g/dl)

or

Hypertonic Saline → better outcomes



Intermittent IV Bolus

Continuous IV Infusion

Efficacy ?? → **Similar efficacy**

Safety ?? → **Continuous IV is safer** *(less ototoxicity)*

Intermittent IV Bolus

Start with SINGLE effective dose

Raise up till MAXIMUN effective dose

according to clinical response

Continuous IV infusion

Continuous IV infusion should not be tried in patients who have not responded to repeated bolus doses

(up to maximum effective dose)

Start Thiazides if:

1- History of chronic use of loop diuretics

2- Partial diuretic response

Add Spironolactone if:

1- HF: NYHA Class III/IV

2- With or at risk of hypokalemia

Monitoring

Lab, Radiology & Clinically

Urology & Nephrology Open Access Journal

UNOAJ

Review Article Volume 1 Issue 2 - 2014

Refractory Edema with Congestive Heart Failure Stepwise Approaches Nephrology Perspectives

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Received: October 16, 2014 | **Published:** November 13, 2014

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Citation: Gawad MA (2014) Refractory Edema with Congestive Heart Failure Stepwise Approaches Nephrology Perspectives. Urol Nephrol Open Access J 1(2): 00011.

Thank You

Gawad